"DRUG UTILIZATION STUDY OF DRUGS PRESCRIBED IN COVID AND NON-COVID RESPIRATORY PATIENTS IN THE DEPARTMENT OF PULMONARY MEDICINE AT A TERTIARY CARE TEACHING HOSPITAL, DELHI NCR"

Thesis submitted to

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UTTAR PRADESH,

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For the award of the Degree of

"DOCTOR OF MEDICINE (M.D.)"

In the Speciality of

PHARMACOLOGY

SANTOSH DEEMED TO BE UNIVERSITY

(Established u/s 3 of UGC Act, 1956)

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INTRODUCTION

A drug is a chemical substance, typically of known structure, which, when administered to a living organism, produces a biological effect. In modern medicine, drugs are usually prescribed in a standard format, known as the prescription. WHO recommends that apart from containing the patient details, a good and complete prescription should clearly mention the drugs in uppercase, legible handwriting; the drugs in question should have a rational behind their use; contain the strength, dosage instruction and total amount and contain the prescribers name, contact details, signature and registration. Evaluating prescriptions comes under the purview of Drug Utilization Studies.[i]

Studies for Drug Utilization began in the mid to late 1960s. Initially taken up by researchers in Northern Europe.[ii,iii] A WHO symposium in 1969 highlighted the need for an internationally accepted classification system for drug utilization studies.[iv] As a result, the Drug Utilization Research Group (DURG) was established and entrusted with the development of internationally applicable methods for Drug Utilization Research (DUR). WHO defines drug utilization research as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences".

Drug Utilization studies can be classified as either descriptive or analytical. The primary goal of a DUR is to identify the pattern, quality, determinants and outcomes of drug use. WHO recommends use of its core indicators, which are primarily divided into prescription indicators, patient care indicators and facility indicators. Core indicators constitute a basic number of indicators from a pool of drug use indicators. These indicators are highly standardized and do not vary by national laws and regulations. They are recommended by the WHO for inclusion in any

drug use study. Although the core indicators do not evaluate all the aspects of drug utilization, they provide a quick and reliable assessment method for the critical aspects of the pharmaceutical use in healthcare.

Pulmonary disease in India is widespread. Ghoshal et al[v] reports that more than 35% of the patients in their study were diagnosed with a combination of four or more respiratory diseases, with asthma being the most common followed by allergic rhinitis. Salvi et al[vi] comments that *"India has a disproportionately high burden of chronic respiratory diseases."* In thje same article it was pointed out that COPD prevalence increased by almost 1% and asthmas went up as high as 3% between 1990 and 2016. India has a huge burden of Tuberculosis, particularly in April-June.[vii] Chowdhury et al[viii] showed peak seasonal variation of Tuberculosis from March to June. Given the situation in India, there has been a dearth of study regarding the drug utilization and rationale of the same.

Of the few studies that have taken in to considerations, respiratory diseases, most have chosen to omit COVID-19. Although it can be said that patient care took precedence over research during the pandemic, retrospective drug utilization study have not been carried out in India. Vinutna et al[ix], studying the use of drugs in acute respiratory illnesses in Bhimavaram, India, found that An average of 5.1 medicines per prescription was noted and 20% of total population were prescribed one or more antibiotics. Amoxicillin+clavulanic acid was the most commonly prescribed FDC (n=13). H2 blocker on the other hand was the highest prescribed non-antibiotic drug (16%). Beg et al[x] studied the prescription trends in Respiratory tract infections in Dehradun, India. They reported that an antibiotic (56.56%) was the most commonly prescribed drug, followed by

bronchodilators (13.8%) and corticosteroids (12.93%). Most of the drugs were oral (52.61%), while FDC (13.24%) was preferred over single dose whenever available.

In light of the above situations, the present study aims to understand the patterns of drug utilization with a special emphasis on the economic aspects of prescriptions provided in the Pulmonary Medicine OPD of Santosh Medical College and Hospital, Ghaziabad, UP.

REVIEW OF LITERATURE

A drug is a chemical substance, typically of known structure, which, when administered to a living organism, produces a biological effect. Drugs are derived from natural resources or produced synthetically. Drugs, much like the evolutionary timeline has had a parallel evolution[xi]. In the wild, primates have been observed to take herbal and clay medicines. Newton suggested that such a *'primate pharmacopeia'* may be of essence in understanding the evolution of medicine.[xii]

Studies for Drug Utilization began in the mid to late 1960s. Initially taken up by researchers in Northern Europe[ii,iii] , Engel et al[xiii] studying the pattern and usage of drugs in multiple European countries highlighted the importance of comparing drug use between different countries and regions. A WHO symposium in 1969 highlighted the need for an internationally accepted classification system for drug utilization studies.[iv] As a result, the Drug Utilization Research Group (DURG) was established and entrusted with the development of internationally applicable methods for Drug Utilization Research (DUR). WHO states that *"...The ultimate goal of drug utilization research must be to assess whether drug therapy is rational or not."*

Detailed comparisons of the drug utilization data obtained from different countries were difficult and at times impossible because the source and form of the information varied between them. To overcome such difficulties, agreed daily dose[xiv] and defined daily dose was developed.[xv] The average maintenance dose of the drug when used on its major indication in adults is defined as

the Defined Daily Dose of a drug. Czechoslovakia became the first country to adopt DDD[xvi], while Norway became the first to adopt a national list of DDDs.[xvii]

DRUG UTILIZATION RESEARCH[xviii]

WHO defines drug utilization research as *"the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences".*

Drug Utilization study may be categorized further as:

- **Descriptive Studies:** to describe patterns of drug utilization and to identify problems deserving more detailed studies.
- **Analytical Studies:** to link data on drug utilization to figures on morbidity, outcome of treatment and quality of care with the ultimate goal of assessing whether drug therapy is rational or not.

Drug utilization studies often employ various sources of information that focus on drugs such as aggregate data from wholesale and prescription registers. It aims to define insights into the following[xix]:

- **Pattern of use:** extent, profile and trends in drug use
- **Quality of use:** compares actual choice of drug, drug cost, drug dosage, drug interactions, and adverse effects to national prescription guidelines
- **Determinants of use:** sociodemographic, prescriber and drug characteristics
- **Outcomes of use:** benefits, adverse effects and economic consequences.

With the gain of the above insights, WHO recommends that DUS can achieve rational use of drugs, defined as *"the prescription of a well-documented drug at an optimal dose, together with the correct information, at an affordable price."*

Thus, the possible avenues of a Drug Utilization Study can be summarized as:

DESCRIPTION OF DRUG USE PATTERN

Drug use patterns chiefly enables the estimation of patients exposed to specified drugs within a given time period. This can then in turn be used to describe the prevalence or incidence of the drug used. This can be further broadened to include a certain moment or area, and is extremely useful to understand the trends if used in a continuous evaluation system. A major implication of these descriptive is the use, overuse or under usage of a particular drug and its alternatives in an epidemiological study of disease, and recommend or amend existing treatment protocol based on the same. A major use of drug utilization pattern has been the development of indicators such as DU90%[xx] which reflects the number of drugs that account for 90% of drug prescriptions.

EARLY DETECTION OF IRRATIONAL USE

Geographical differences and changes in drug use over time may have medical, social and economic implications both for the individual patient and for society, and should therefore be identified, explained and, when necessary corrected. Patterns of drug use are compared with current guidelines, and wherever discordance is seen, hypothesis can be formed that set the agenda for further investigations.

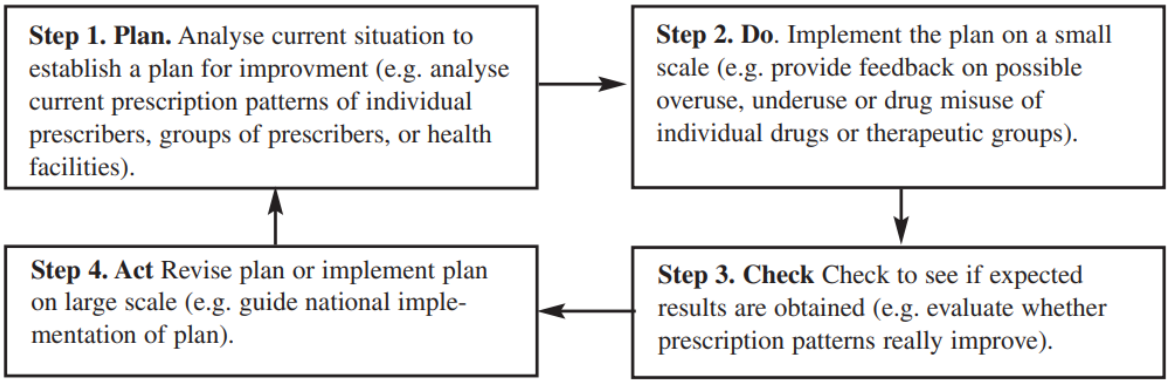
INTERVENTIONS TO IMPROVE RATIONAL USE

Often, prescribers may switch to other drugs which have not been subjected to drug utilization studies, but are otherwise, undesirable. Drug utilization studies may include steps to avoid such undesirable patterns of drug use. This often evaluates and monitors local formularies, information campaigns and regulatory policies.[xxi] WHO encourages the inclusion of alternative drugs to such studies to assess the full impact of a proposed measure. Further, DUS can help in evaluating the extent to which the promotional activities of the pharmaceutical industry affect the patterns of drug use.

QUALITY CONTROL

WHO recommends the use of Quality control cycle to exercise benchmarking and quality of the drugs provided on a national or regional scale.

Fig 1: Figure showing WHO quality control cycle[xviii]


Step 1. Plan. Analyse current situation to establish a plan for improvment (e.g. analyse current prescription patterns of individual prescribers, groups of prescribers, or health facilities).
Step 2. Do. Implement the plan on a small scale (e.g. provide feedback on possible overuse, underuse or drug misuse of individual drugs or therapeutic groups).
Step 3. Check Check to see if expected results are obtained (e.g. evaluate whether prescription patterns really improve).
Step 4. Act Revise plan or implement plan on large scale (e.g. guide national imple-mentation of plan).

DRUG POLICY DECISIONS

Estonia gained autonomy from the Soviet Union in 1991. Post-Soviet Estonia became the proverbial petri dish for Drug Utilization Studies (DUS) and the protocols and rules that would be hence laid out. Owing to the unavailability of information related to sale and quantity of drugs

in Estonia, no rationale for regulating the drug market was in place. Moreover, this was complicated by the near absence of a feedback reporting system. From 1992-1994, a national drug classification system was developed, tested and validated by the wholesale drug market. Reviews and feedback were provided for drug utilization and by the late 1990s Estonia not only had a national drug policy, but was a country which had adopted DDD. Drug utilization studies were used to stop the import and use of some hazardous products, such as phenacetine, older sulphonamides and pyrazolones, after clarifying and explaining the reasons for the same.

MEASUREMENT OF DRUG UTILIZATION[xxii]

DEFINED DAILY DOSE (DDD)[xxiii]

As per the WHO, *"DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults."* DDD is a unit of measurement, and is not a recommendation for prescription doses. Doses for patients may vary greatly to DDD as dosage is often dependent on the severity of disease, and the individual pharmacokinetics of the drug. In fact, DDD may even be a dose that is seldom prescribed, because it is an average of two or more commonly used dose sizes. DDD is often expressed as number per 1000 inhabitants per day, or, for inpatient data, numbers per 100 bed-days.

DDDs per 1000 inhabitants per day

DDDs per 1000 inhabitants per day are usually derived from sales or prescription data. It provides a rough estimate of the proportion of the study population treated daily with a particular drug or group of drugs. For example, the figure 10 DDDs per 1000 inhabitants per day indicates that 1% of the population on average might receive a certain drug or group of drugs daily. DDDs

are most effective when used for drugs used in chronic disease, as compared to acute or emergency cases. DDD are usually calculated for the entire population, and includes all age groups. A major drawback of this method is the non-standardization of data. For example, drugs that are seldom used in patients below the age of 40 may provide much lower DDDs, than what the target demography is. To correct for differences in utilization, simple age adjustments can be made by using the number of inhabitants in the relevant age group as the denominator.

DDDs per 100 bed-days[xxiv]

DDDs per 100 bed-days are used mainly for in patient data. Bed days are usually adjusted for occupancy rate of the sample population, as it may vary based on geographical regions. For example, 70 DDDs per 100 bed-days of hypnotics provide an estimate of the therapeutic intensity and suggests that 70% of the inpatients might receive a DDD of a hypnotic every day. This metric is not used extensively, and is reserved for benchmarking of hospitals.

PRESCRIBED DAILY DOSES (PDD)[xv]

The prescribed daily dose (PDD) is the average daily dose prescribed, as obtained from a representative sample of prescriptions. PDD can be determined from studies of prescriptions or medical records and are usually different between countries, and even different geographical area within a country. The PDD will also often differ for different indications of the same drug. Being the older metric, PDD varies significantly from the Defined Daily Dose (DDD) concept, whereby, although DDD provides a more uniform and standardized data, PDD may reflect the trends in more detail. The two metrics give different results for the relative use of the two groups of a drug because of the different relationship between the PDDs and the DDDs for the two drug groups. While DDD is a metric that can be used to compare between multiple study groups, PDD

indicates the average daily amount of a drug that is actually prescribed. Another cause of obsolescence for PDD was the necessity of pharmacoepidemiological data for interpretation. PDD is also affected by disease severity. WHO further comments that, *"It should be noted that the PDD does not necessarily reflect actual drug utilization. Some prescribed medications are not dispensed, and the patient does not always take all the medications that are dispensed."*

OTHER METHODS

Both DDD and PDD, although they provide a thorough throughput of data and standard comparison metrics, are expensive studies that cannot be undertaken on a daily basis. As already stated, these studies are essential in comparing trends, but for an acute snapshot of the utilization, usually simpler quantification methods, such as common physical units (grams, numbers, litres etc.) are used. The popular methods are as follows:

- Grams of active ingredient
- Number of tablets per prescription
- Number of prescriptions

SOURCES OF DATA FOR DUS[xxv]

WHO recommends that Drug use monitoring should involve a chain in the following sequence: drug acquisition, storage, distribution, prescribing, patient compliance and the review of outcome of treatment.

Each of these steps is an important waypoint for understanding drug utilization. Data is usually collected at national, regional and local health facility or household level and may be derived

from quantitative or qualitative studies. Quantitative data may be routinely collected data or obtained from surveys, whereas qualitative data is used to describe the present situation and the trends in drug prescribing and drug use. The following are the most common sources of data for DUS:

- National Databases
- Corporate Databases
- Drug Regulatory Agencies
- Supplier of Drugs
- Data Variables
    - Practice Data
        1. average number of drugs per prescription
        2. percentage of drugs prescribed by generic name
        3. percentage of encounters resulting in prescription of an antibiotic
        4. percentage of encounters resulting in prescription of an injection
        5. percentage of drugs prescribed from essential drugs list or formulary
        6. average drug cost per encounter
    - Dispensing Data
        1. drug(s) prescribed
        2. dose(s) prescribed
        3. average number of items per prescription
        4. percentage of items prescribed that were actually supplied (availability indicator)

5. percentage of drugs adequately labelled
6. quantity of medications dispensed
7. cost of each item or prescription

DRUG USE EVALUATION

Drug utilization review, is a system of continuous, systematic, criteria-based drug evaluation that ensures the appropriate use of drugs. The final step of a DUS involves forming a review and feedback-based system to assess the appropriate indications, drug selection, dose, route of administration, duration of treatment and drug interactions, along with treatment outcomes. The objectives of typical DUS are as follows:

- ensuring that drug therapy meets current standards of care
- controlling drug cost
- preventing problems related to medication
- evaluating the effectiveness of drug therapy
- Identification of areas of practice that require further education of practitioners.

WHO DRUG USE INDICATORS[xxv]

Drug use indicators are used to measure specific aspects of the behaviour of health providers in health facilities in a reproducible manner, while ameliorating the effects of observer biases.[xxvi] Drug Use indicators were developed as a result of studies in Yemen[xxvii] and Uganda[xxviii], which pioneered some of the early indicators. The methodology was further tested in Indonesia, Bangladesh and Nepal. Following set of reviews, and a series of final field tests in Nigeria and Tanzania in 1992, the present set if indicators were formed[xxix]. The techniques developed by

WHO are such that such indicators can be measured in a standard way by individuals without special training or access to many resources. The major objective of WHO Drug use indicators is to prioritize and focus subsequent efforts to correct the potential problems in drug use. WHO however, cautions that there is no "gold standard" for assessing the correct behaviour of pharmaceutical treatment. Rather, the indicators are intended to stimulate further questioning and guide subsequent actions.

Drug use indicators are used to measure performances in three general areas:

1. Prescribing practices by Health providers
2. Clinical consultation and pharmaceutical dispensing
3. Availability of facility specific factors.

Core indicators constitute a basic number of indicators from a pool of drug use indicators. These indicators are highly standardized and do not vary by national laws and regulations. They are recommended by the WHO for inclusion in any drug use study. Although the core indicators do not evaluate all the aspects of drug utilization, they provide a quick and reliable assessment method for the critical aspects of the pharmaceutical use in healthcare. Core indicators are most commonly used to identify issues with a particular drug use, which warrants examination in more detail. All of the data needed to measure core indicators are collected from medical records or direct observations at individual health facilities.

Table 1: WHO drug use core indicators

Group	Indicator
Prescribing Indicators	Average number of drugs per prescription
	Percentage of drugs prescribed by generic name

	Percentage of encounters resulting in prescription of an antibiotic
	Percentage of encounters with an injection prescribed
	Percentage of drugs prescribed from essential drugs list or formulary
Patient Care Indicators	Average consultation time
	Average dispensing time
	Percentage of drugs actually dispensed
	Percentage of drugs adequately labelled
	Patients' knowledge of correct dosage
Facility Indicators	Availability of copy of essential drugs or formulary
	Availability of key drugs

PRESCRIBING INDICATORS

Prescribing indicators measure the performance of healthcare providers. These indicators are based on the practices observed in a sample of clinical encounters taking place at the outpatient health facilities. Signs and symptoms are not required for the core prescribing indicators. While the core indicators do not measure specific disease and their treatment patterns, they measure general prescribing tendencies, independent of diagnosis.

- Average number of drugs per prescription
    - **Purpose:** To measure the degree of polypharmacy.
    - **Calculation:** Average, calculated by dividing the total number of drug products prescribed, by number of encounters.
- Percentage of drugs prescribed by generic name
    - **Purpose:** To measure the tendency to prescribe by generic name.

    - **Calculation:** Percentage, calculated by dividing the number of drugs prescribed by generic name by total number of drugs prescribed, multiplied by 100.
- Percentage of encounters with an injection prescribed/Percentage of encounters resulting in prescription of an antibiotic
    - **Purpose:** To measure the overall use of two important but commonly overused and costly form of drug therapy.
    - **Calculation:** Percentage, calculated by dividing the number of encounters in which an injection and/or antibiotic is prescribed by total number of encounters, multiplied by 100.
- Percentage of drugs prescribed from essential drugs list or formulary
    - **Purpose:** To measure the degree to which practices conform to national drug policies.
    - **Calculation:** Percentage, calculated by dividing the number of products prescribed which are listed in the essential drugs list by total number of drug products prescribed, multiplied by 100.

PATIENT CARE INDICATORS

Patient care indicators addresses key ascpefcft6s of what patients experience at health facilities. The time spent by prescribers and dispensers with each patient sets important limits o the potential quality of diagnosis and treatment. WHO recommends that patients are supposed to receive, at the least, well labelled medications, and should have aq clear understanding on how to take each drug.

FACILITY INDICATORS

Adequate supply of essential drugs and access to unbiased information about such are the key components of rational drug prescription.

PROFILE OF PATIENTS IN A PULMONARY CLINIC

India has a huge burden of respiratory diseases. Ghoshal et al[v] reports that more than 35% of the patients in their study were diagnosed with a combination of four or more respiratory diseases, with asthma being the most common followed by allergic rhinitis. COPD and asthma contributed to three-fourth and one-fifth of DALYs in 2016, with the highest rates seen in Rajasthan and Uttar Pradesh.[xxx] Moreover, India has a huge burden of Tuberculosis, particularly in April-June.[vii] A similar study by Chowdhury et al[viii] showed peak seasonal variation of Tuberculosis from March to June. A major study by Dasgupta et al[xxxi], constituting of 2000 patients was taken up in 2006. Asthma was once again reported as the highest burden, followed by COPD, infections and soft tissue disorders. Surprisingly, Tuberculosis was seen as the 5th most common diagnosis, which the author attributed to the limited data owing to the study being carried out in a private healthcare setting. COPD data is usually scanty in India, while disorders like ILD and Sarcoidosis have negligible interest in epidemiology.[xxxii,xxxiii] A similar study by Dubey et al[xxxiv] in Bhopal however, reported that infections carried the greatest burden followed by Asthma and other obstructive diseases.

It is of interest to note that despite being an epidemic, OPD data for COVID-19 cases are usually scant. Although myriad epidemiological research has been done regarding COVID-19, a thorough search of databases did not yield satisfactory information regarding the profile of COVID-19 patients in the OPD.

PREVIOUS STUDIES

Beg et al,[x] studied the prescription trends in Respiratory tract infections in Dehradun, India. They reported that an antibiotic (56.56%) was the most commonly prescribed drug, followed by bronchodilators (13.8%) and corticosteroids (12.93%). Most of the drugs were oral (52.61%), while FDC (13.24%) was preferred over single dose whenever available. 8.32 drugs were prescribed per prescription. 49.47% drugs were prescribed from national essential medicine list 2015, and 88.72% of the drugs were prescribed with brand names.

Bandyopadhyay et al[xxxv] conducting a study in a tertiary care hospital in rural West Bengal reported that on average, 2.5 medicines were prescribed per prescription, with 95.26% being under their generic name and 95.79% were from the essential drug list. The average consultation time was 150.0 seconds and average dispensing time was 81.5 seconds. Antibiotics (47.83%) was the majorly prescribed drug class. 2.83% of the drugs prescribed were injectables. 91.67% of the patients reported to have a knowledge of their prescribed drugs.

Sun et al[xxxvi] studying drug utilization, disease progression, and adverse events among 165 COVID 19 patients reported that antivirals, antibacterials, glucocorticoids, and traditional Chinese medicine (TCM) were administered to 92.7%, 98.8%, 68.5%, and 55.2% of patients, respectively. The total kinds of drugs administered to the severe subgroup were 11 more than the non-severe subgroup, regardless of comorbidities. Antiviral therapy + glucocorticoids + TCM (49.1%) and Antiviral therapy + glucocorticoids (13.9%) were the two most commonly prescribed drug combinations. Severe cases received more glucocorticoids (88.5%) than non-severe subgroup. 13 patients (7.9%) had elevated liver enzymes, and 49 patients (29.7%) presented with worsening kidney function during the follow-up.

AIM

To study the drug utilization pattern of drugs prescribed in a patients of respiratory disorders in the department of pulmonary medicine.

OBJECTIVES

- To assess the pattern of drugs prescribed in the department of pulmonary medicine.
- To assess the most frequently prescribed drugs and their doses & duration for conditions including COPD, Tuberculosis, Bronchial Asthma, pneumonia,Covid-19 and post COVID fibrosis.
- To assess average number of drug per prescription
- To assess cost analysis per prescription.
- To assess percentage of drugs prescribed by generic name.
- To assess ADR if any observed.

MATERIALS AND METHODS

The present study titled “Drug utilization study of drugs prescribed in covid and Non covid respiratory patients in the department of pulmonary medicine at a tertiary care teaching hospital” was conducted among the patients attending pulmonary medicine OPD at Santosh Medical College and Hospital, Ghaziabad, UP.

Ethical clearance was obtained from the Institutional Ethics Committee of Santosh Medical College and Hospital, Ghaziabad. The confidentiality and anonymity of the study participants were maintained by the researcher.

Study Design: It was an observational cross-sectional type of study conducted in the department of Pharmacology and Pulmonary medicine at Santosh Medical College and Hospital, Ghaziabad, UP.

Study period: - Period of study was 12 months.

Data collection: Prescriptions of all patients attending pulmonary medicine OPD which met the inclusion criteria were included in the study.

Sample size:

The sample size is determined by using the following formula:

$$N = \frac{z^2 p(1-p)}{d^2}$$

Where:
n = sample size
P = estimate of the proportion of prescriptions with an inappropriate prescription pattern,0.5 since there is no research finding regarding estimate of inappropriate drug prescribing pattern in Santosh Hospital
d = margin of sampling error tolerated, 0.04

Z = the standard normal value at confidence interval of 98%, z value= 2.33

$$\text{The sample size was } n = \frac{(2.33)^2\,(0.5)(1-0.5)}{(0.04)^2} = 849$$

The sample size thus calculated was 849. This was rounded off to the final sample size of 1000.

So, the final sample size was 1000.

Inclusion Criteria:

All prescriptions prescribed in the OPD of Pulmonary Medicine, including all ages.

Exclusion Criteria:

1. Critically ill patients: - patients having comorbidities like CAD, CKD on MHD, saturation less than 90%,

Variables under study:

The following data were collected, assessed and analyzed. Enlisted below:

- Socioeconomic Variables
    - Age
    - Gender
    - Socioeconomic status
    - Literacy
    - Address (Urban/Rural) Religion
    - Occupation
    - Race (Tribal/Non-Tribal)
- Prescription Variables

- Diagnosis
- Patient particulars
- History
- Legibility
- Directions of Use
- Number of Drugs
- Duration of Treatment
- Number of Tests
- Total cost of prescription
- Name and Registration of Prescribing physician

➢ Drug Variables

- Drug Class
- Type of Drug (Generic/Retail)
- Active Molecule
- Single/Fixed Dose Combination
- Route
- Dosage
- Duration
- Directions
- Cost of pack
- Drug availability (Only institutional pharmacy considered)

Data Analysis:

Collected data from all participants were checked for consistency and completeness. Data were entered in Microsoft Excel data sheet for analysis. Data were organized and presented using the principles of descriptive statistics as tables and diagrams. Mean and standard deviations (SD) were calculated for continuous data. An Independent sample t-test was done to compare continuous variables and chi-square test was done to compare between categorical ones. IBM statistical package for Social Sciences (SPSS) version 21.0 was used for data analysis. A significance value (p-value) < 0.05 was considered significant.

RESULTS

Figure 1: Flow chart of patients recruited in the study (n=1280)

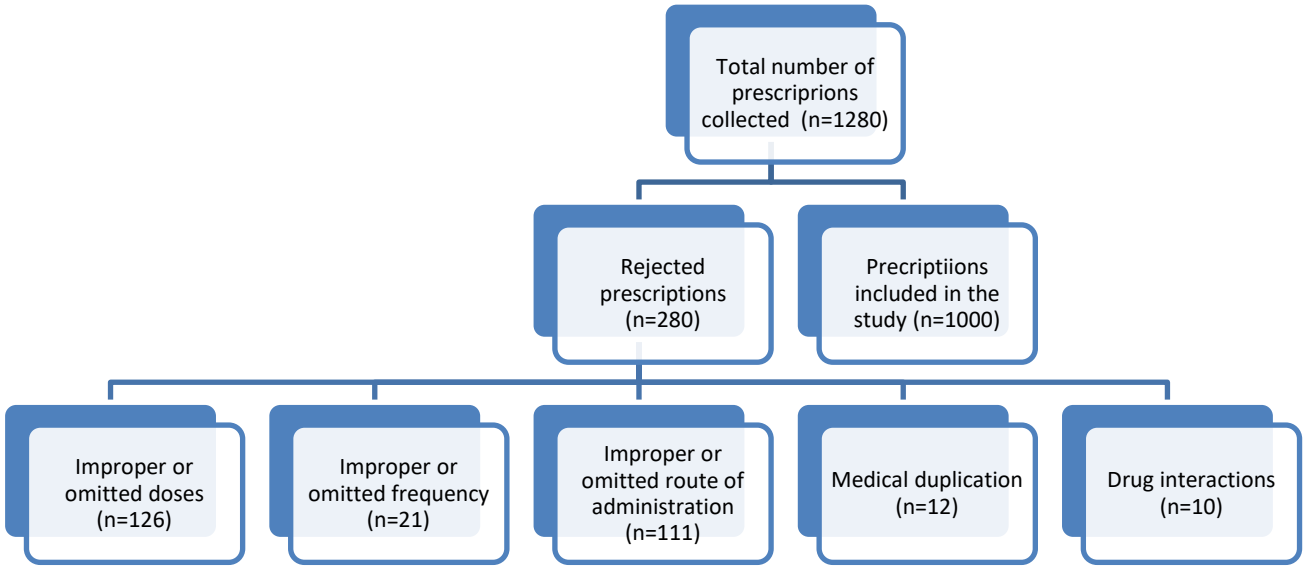
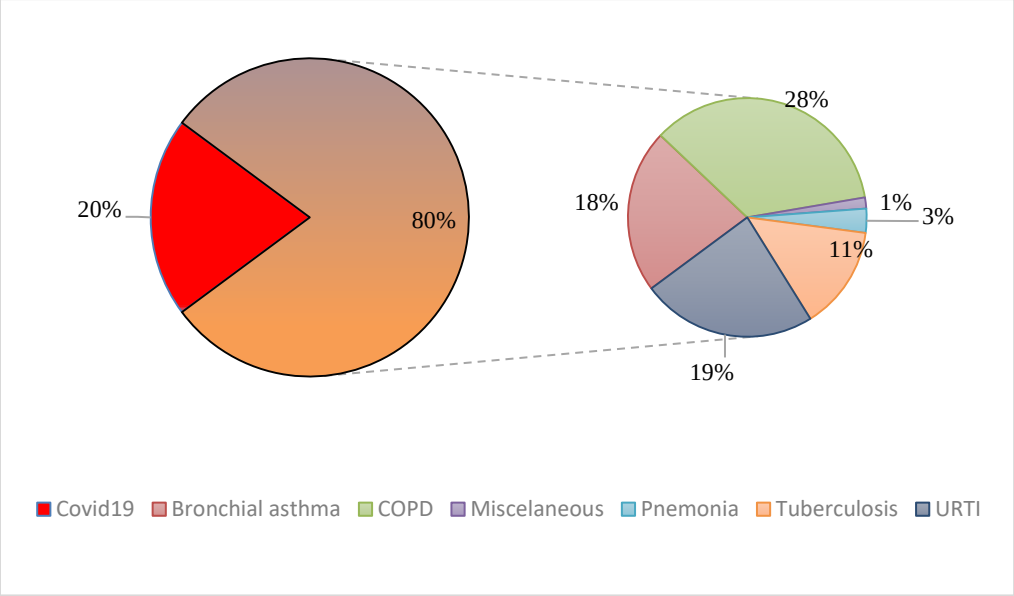

Total number of prescriprions collected (n=1280)
Rejected prescriptions (n=280)
Precriptiions included in the study (n=1000)
Improper or omitted doses (n=126)
Improper or omitted frequency (n=21)
Improper or omitted route of administration (n=111)
Medical duplication (n=12)
Drug interactions (n=10)

Table 2: Distribution of prescriptions based on covid and NCRP (n=1000)

Prescriptions	Frequency	Percent
Covid	203	20.3
NCRP	797	79.7
Total	1000	100.0

**NCRP – Non Covid Respiratory Patients*



Miscellaneous includes interstitial lung diseases, lung masses for investigation

Figure 2: Pie in pie chart showing the distribution of the study population based on the diagnosis (n=1000)

Figure shows the categorise wise break up opd patients attending the study setting. One-fifths (20.3%) of the prescriptions included in the study were from covid patients, while the others were from non-covid respiratory patients. Among them the commonest prescriptions (28%) were from COPD patients, followed by URTI (19%). The lowest number of patients had miscellaneous diagnosis like interstitial Lung disease, lung cancers etc.

Majority (79.7%) of the prescriptions are from NCRP (non-covid respiratory patients), while 20.3% of the prescriptions are from covid patients.

Table 3: Distribution of age groups in the prescriptions based on covid and non-covid patients

(n=1000)

Age groups (years)	Total prescriptions N (%)	NCRP N (%)	Covid patients N (%)	Chi square test	p value
18-30	92 (9.4)	55 (6.9)	37 (18.2)	51.55	0.000*
30-45	224 (22.4)	177 (22.2)	47 (23.2)		
45-60	191 (19.1)	134 (16.8)	57 (28.1)		
>60	493 (49.3)	431 (54.1)	62 (30.5)		
Total	1000 (100)	797 (100)	203 (100)		

*Statistically significant

Among the total prescriptions, most were more than 60 years of age group (49.3%), while the least proportion of patients was in the 18-30 years age group (18.2%). Among both covid and non-covid respiratory patients, the highest proportion of patients were more than 60 years of age (30.5% and 54.1% respectively), while the lowest proportion of patients were seen in 18-30 years of age group in both non-covid and covid patients (18.2% and 6.9% respectively). There was a significant difference between the age groups and the proportion of prescriptions between covid and non-covid patients.

Table 4: Descriptive of age among total prescriptions and prescriptions for covid and non-covid patients

(n=1000)

Age (years)	Total prescriptions	NCRP	Covid patients	Independent sample t test	p value
Minimum	18	18	22		
Maximum	82	82	78		
Mean	55.9	57.5	49.2	6.08	0.000*
Standard deviation	17.7	17.5	16.8		

*Statistically significant

The mean (standard deviation) age of patients in total, non-covid and covid prescriptions were 55.9 (17.7), 57.5 (17.5) and 49.2 (16.8) years respectively. The minimum age of patients among the total, non-covid respiratory prescriptions and covid prescriptions were 18, 18 and 22 years respectively, while the maximum age of patients among the total, non-covid respiratory prescriptions and covid prescriptions were 82, 82 and 78 years respectively.

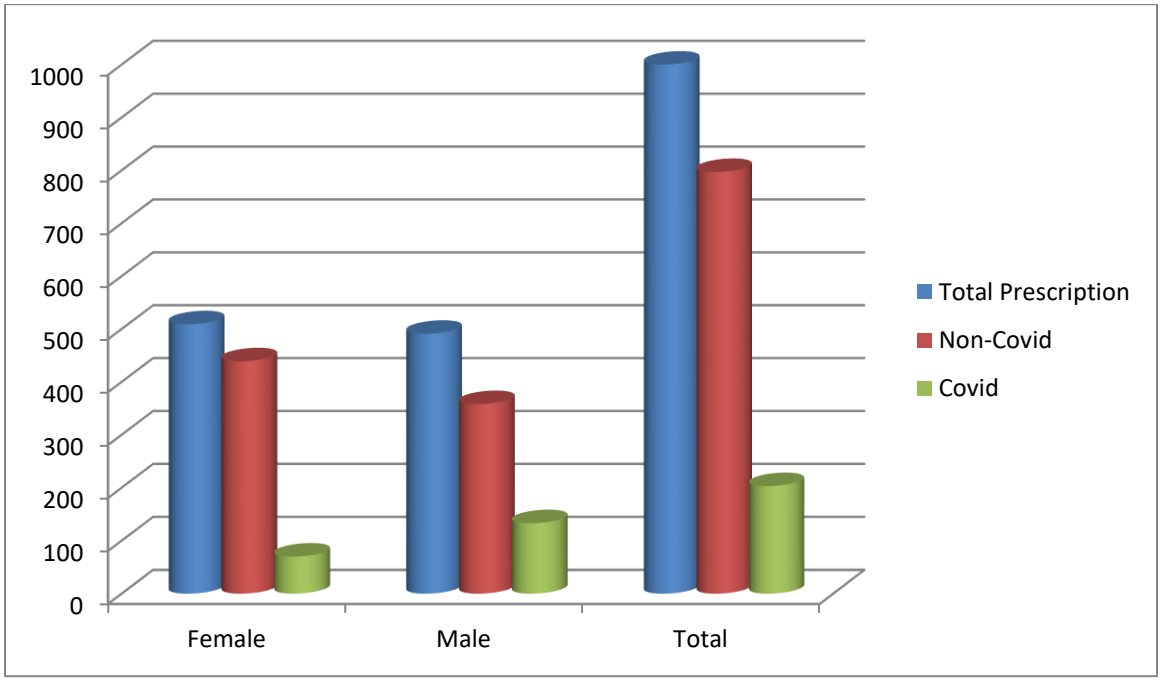
Non covid respiratory patients were significantly older than covid patients.

Table 5: Descriptives of gender in total prescriptions and prescriptions for covid and non-covid respiratory patients

(n=1000)

Gender	Total prescriptions N (%)	NCRP N (%)	Covid patients N (%)	Chi square test	p value
Female	509 (50.9)	439 (55.1)	70 (34.5)	27.47	<0.001*
Male	491 (49.1)	358 (44.9)	133 (65.5)		
Total	1000 (100)	797 (100)	203 (100)		

*Statistically significant



Among the total prescriptions, most were females (50.9%). Among non-covid respiratory prescriptions majority were female (55.1%) while among covid prescriptions majority were males (65.5%). There was a statistically significant difference in the gender of patients between prescriptions of covid and non covid respiratory prescriptions

Table 6: Distribution of prescriptions based on the presence of co-morbidity (n=1000)

Co-morbidities	Total prescriptions N (%)	NCRP N (%)	Covid prescriptions N(%)
No co-morbidity recorded	521 (52.1)	439 (55.1)	82 (40.4)
Asthma	15 (1.5)		7 (3.4)
COPD	25 (2.5)		13 (6.4)
Diabetes	166 (16.6)	141 (17.7)	21 (10.4)
Hypertension	253 (25.3)	176 (22.1)	77 (37.9)
Hypothyroid	17 (1.7)	38 (4.7)	3 (1.5)
Rheumatoid arthritis	3 (0.3)	3 (0.4)	0
Total	1000 (100)	797 (100)	203 (100)

*Proportions may add upto more than 100 because of the presence of more than one co-morbidity in a patient

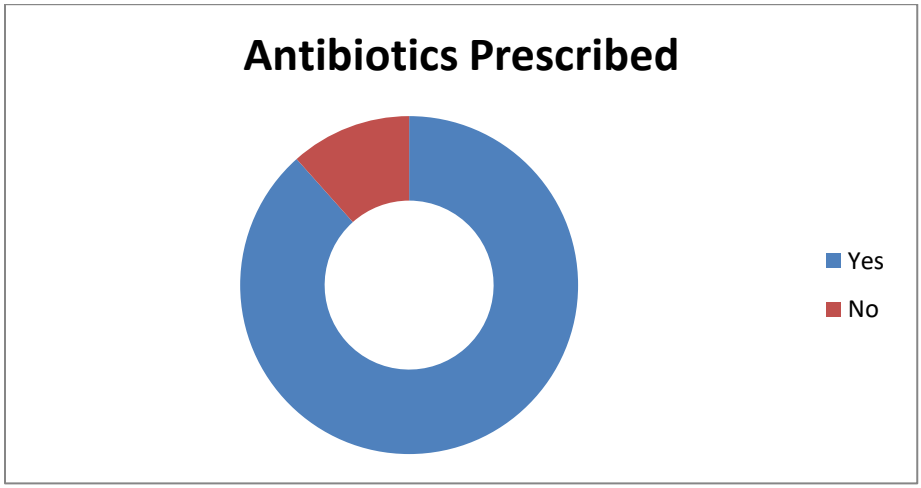
The most common recorded co-morbidity among all prescriptions was hypertension (25.3%), while the least common was Rheumatoid arthritis (0.3%). Among non-covid respiratory prescriptions the commonest recorded co-morbidity was hypertension (22.1%) followed by diabetes (17.7%). Among covid patients also the commonest comorbidity was hypertension (37.9%) and diabetes (10.4%).

Table 7: Antibiotics prescribed in total prescriptions and prescriptions for covid and non-covid respiratory patients

(n=1000)

Antibiotics prescribed	Total prescriptions N (%)	NCRP N (%)	Covid patients N (%)	Chi square test	P value
No	116 (11.6)	113 (14.2)	3 (1.5)	25.45	0.000*
Yes	884 (88.4)	684 (85.8)	200 (98.5)		
Total	1000 (100)	797 (100)	203 (100)		

*Statistically significant



Antibiotics were prescribed in 88.2% of total, 85.8% of non-covid cases and 98.5% of all covid cases respectively. A significantly higher proportion of prescription from covid patients had antibiotics than patients with non-covid.

Table 8: Class of antibiotics prescribed in total, covid and non-covid respiratory prescriptions

(n=1000)

Class of antibiotics prescribed	Total prescriptions N (%)	NCRP N (%)	Covid prescriptions N (%)	Chi square /p value
No antibiotics prescribed	116 (11.6)	113 (14.2)	3 (1.5)	26.26/ <.001*
Amoxicillin + Clavulanic acid	263 (26.3)	220 (27.6)	43 (21.2)	2.57/ .109
Azithromycin	209 (20.9)	127 (15.9)	82 (40.4)	58.55/ <.001*
Cefpodoxime + Clavulanic acid	68 (6.8)	68 (8.5)	0	18.58/ <.001*
Cefuroxime	3 (0.3)	3 (0.4)	0	0.77/ 0.381
Ciprofloxacin	148 (14.8)	148 (18.6)	0	44.24/ <.001*
Doxycycline	312 (31.2)	112 (14.1)	200(98.5)	228.28/ <.001*
Piperacillin + Tazobactam	6 (0.6)	6 (0.8)	0	1.54/ 0.215
Total	1000 (100)	797 (100)	203 (100)	

*Percentages may add up to more than 100 because of the use of more than 1 antibiotic in every prescription

No antibiotics were prescribed in 11.6%, 14.2% and 1.5% of patients in overall prescriptions, non -covid respiratory prescriptions and covid prescriptions respectively.

No antibiotics were prescribed in 11.6%, 14.2% and 1.5% of patients in overall prescriptions, non -covid prescriptions and covid prescriptions respectively. A significantly higher proportion of patients in the Covid group have been prescribed doxycycline or Azithromycin compared to NCRD. Cefpodoxime + Clavulanic acid, Ciprofloxacin have been prescribed in significantly more patients with NCRP than covid , while there was no statistically significant difference in the prescription of Amoxicillin + Clavulanic acid, Cefuroxime and Piperacillin + Tazobactam between the groups.

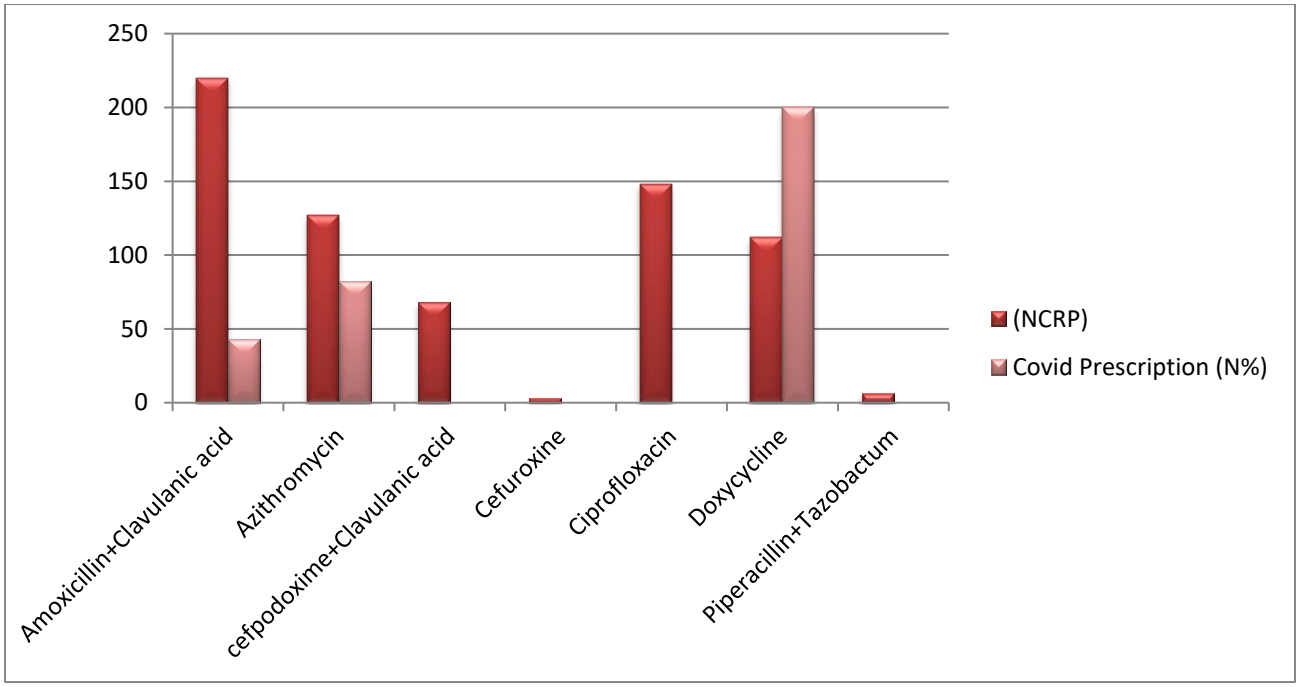


Table 9: Showing the drug utilization of the antibiotics prescribed by a physician for covid and NCRP patients during the study period

Drug Name	ATC Code	WHO DDD	PDD	PDD/WHO DDD RATIO
Azithromycin	J01CR02	0.5	1.217	>1
Doxycycline	J01AA02	0.1	0.2	>1
Amoxicillin-beta lactamase inhibitor	J01CR02	1.5	1.217	<1

PDD/DDD ratio >1 in the study group indicates that there is overdosing of the antibiotics.

Table 10: Classes of drugs prescribed in total prescriptions and prescriptions for covid and non-covid patients

(n=1000)

Classes of drugs prescribed	Total prescriptions N (%)	Non-covid patients N (%)	Covid patients N (%)
Antibiotics	885 (88.5)	682 (85.6)	200 (98.5)
Antivirals	9 (0.9)	0	9 (4.4)
Mucolytics	940 (94)	749 (94)	191 (94.1)
Inhaled Bronchodilators	502 (50.2)	472 (59.2)	30 (14.8)
Oral Bronchodilators	20 (2)	16 (2)	4 (2)
Inhaled Corticosteroids	644 (64.4)	620 (77.8)	24 (11.8)
Oral Corticosteroids	26 (2.6)	11 (1.4)	3 (1.5)
Antitubercular Drugs	112 (11.2)	112 (14.1)	0
Paracetamol	128 (12.8)	120 (15.1)	195 (96.1)
Antacids	317 (31.7)	309 (38.8)	195 (96.1)
Antihistaminic	215 (21.5)	49 (6.1)	166 (81.8)
Vitamins and Zinc	406 (40.6)	246 (30.9)	160 (78.8)
Ivermectin	160 (16)	0	160 (78.8)
Antihypertensive	259 (25.9)	180 (22.6)	79 (38.9)
Oral hypoglycaemic	164 (16.4)	144 (18.1)	20 (9.9)

Overall, the most commonly prescribed drug group was Mucolytics (94%) followed by antibiotics (88.2%), inhaled corticosteroids (64.4%) and inhaled bronchodilators (50.2%).

Among non-covid respiratory prescriptions, the most commonly prescribed drug group was Mucolytics (94%) followed by antibiotics (85.6%), inhaled corticosteroids (77.8%) and inhaled bronchodilators (59.2%). Antitubercular drugs were prescribed in 14.1% of the patients.

Table 11: Number of drugs per prescription among total, covid and non-covid respiratory patient prescriptions

(n=1000)

Number of drugs per prescription	Total prescriptions N (%)	NCRP N (%)	Covid prescriptions N (%)
1-2	1 (0.1)	1 (0.1)	0 (0.0)
3-4	296 (29.6)	248 (31.1)	48 (23.7)
5-6	509 (50.9)	396 (53.7)	113 (55.6)
7-8	169 (16.9)	130 (16.3)	39 (19.2)
>8	8 (0.8)	5 (0.6)	3 (1.5%)
Total	1000 (100)	797 (100)	203 (100)

Overall, the most prescriptions had 5-6 drugs (50.9%), followed by 3-4 drugs (29.6%). Only0.1% of prescriptions had 1-2 drugs while 16.9 % had 7-8 drugs per prescription. For non-covid patents, the most prescriptions had 5-6 drugs (53.7%), followed by 3-4 drugs (31.1%). Only 16.3% of prescriptions had 7-8 drugs while 0.1% had 1-2 drugs per prescription. For covid patients, the most prescriptions had 5-6 drugs (55.6%), followed by 3-4 drugs (23.7%), while 19.2% had 7-8 drugs per prescription. None of the prescriptions had 1-2 drugs.

Among prescriptions for covid patients, the most commonly prescribed drug groups were antibiotics and antipyretics (98.5%) followed by antihistaminics (81.1%), ivermectin and vitamins and zinc (78.8%).

Table 12: Descriptive of drugs per prescription on total, covid and non-covid prescription (n=1000)

Number of drugs per prescription	Total prescriptions N (%)	NCRP N (%)	Covid prescriptions N (%)	Independent sample t test	P value
Minimum	1	1	3		
Maximum	9	9	9		
Mean	5.2	5.1	5.5	3.74	0.000*
Standard deviation	1.4	1.4	1.2		

*Statistically significant

The mean (standard deviation) number of drugs per prescription overall, among non-covid prescriptions and covid prescriptions were 5.2, 5.1 and 5.5 respectively. The minimum and maximum numbers of drugs prescribed among all prescriptions were 1 and 9 respectively. There was a significant difference in the number of drugs prescribed between prescriptions of covid and non-covid patients.

Table 13: Descriptive of generic drugs on total, covid and non-covid respiratory prescriptions

(n=1000)

Number of generic drugs per prescription	Total prescriptions N (%)	Non-covid prescriptions N (%)	Covid prescriptions N (%)	Independent sample t test	P value
Minimum	0	0	0		
Maximum	6	5	6		
Mean	1.6	2.3	1.5	10.18	0.000*
Standard deviation	1.0	1.0	1.0		

*Statistically significant

The mean (standard deviation) number of generic drugs per prescription overall, among non-covid prescriptions and covid prescriptions were 2.3(1.0) and 1.5 (1.0) respectively. The minimum and maximum numbers of generic drugs prescribed among all prescriptions were 0 and 6. There was a significant difference in the number of generic drugs prescribed between prescriptions of covid and non-covid patients.

Table 14: The prescribing indicators with the recommended standard values (n=1000)

Indicators	Total prescriptions	Non-covid prescriptions	Covid prescriptions	Standard value*
Drugs prescribed per encounter (mean)	5.2	5.1	5.5	<2.0
Drugs prescribed by generic name (%)	32.1%	29.4%	42.2%	100%
Encounters with antibiotics (%)	88.4	85.8	98.5	<30%
Encounters with injections (%)	Nil	Nil	Nil	<20%
Percentage of drugs from the essential drugs list (%)	100	100	100	100%

*based on Isah AO et al. The development of standard values for the WHO drug use prescribing indicators

Table 15: Adverse Drug reactions in the study population
(n=1000)

Adverse Reaction	Frequency	Percentage
Yes	221	22.1
No	779	77.9
Total	1000	100

*Adverse drug reactions were observed in 22.1% of the total patients.

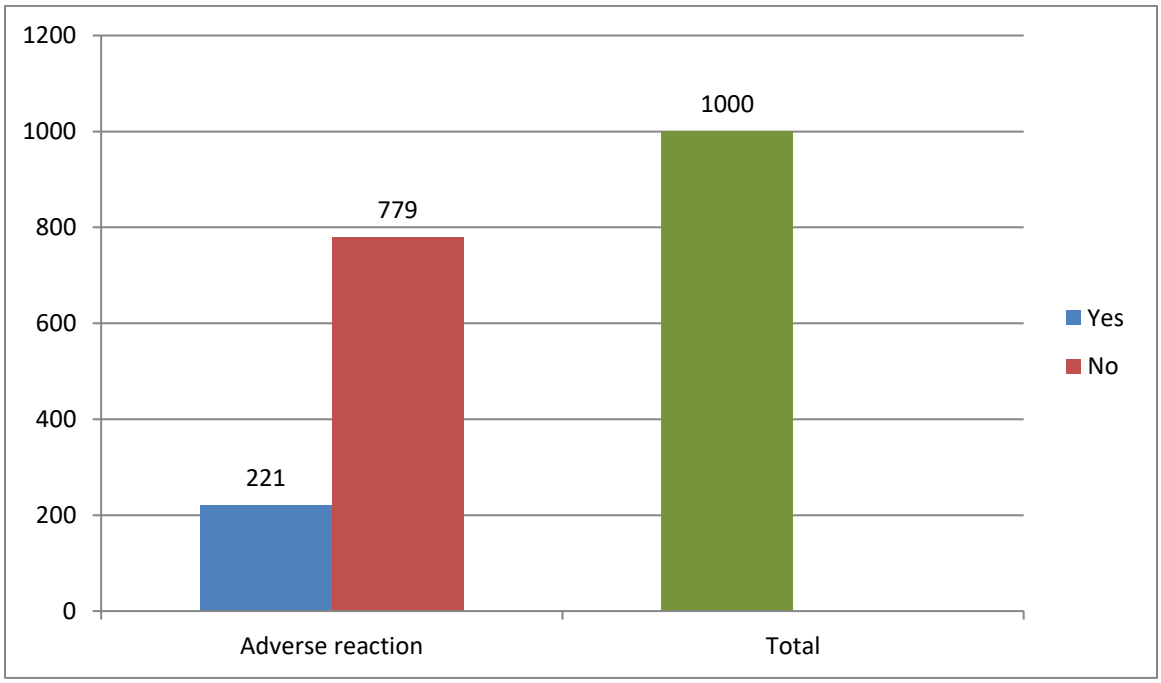


Table 16: Type of ADR Symptoms in prescriptions of covid and NCRP
(n=342)

Types of ADR Symptoms	Frequency	Percentage
Diarrhoea	70	7.0
Nausea/Vomiting	65	6.5
Urticaria	60	6.0
Dizziness	26	2.6
Cough	28	2.8
Difficulty Breathing	9	0.9
Elevated Liver Enzyme	2	0.2
Drowsiness	2	0.2
Palpitations	1	0.1

The commonest side effect recorded on the prescription was diarrhoea (7%), followed by nausea/ vomiting (6.5%), urticaria (6%) and dizziness (2.6%). The east common recorded adverse drug reactions on prescriptions were drowsiness, elevated liver enzymes (0.2%) and palpitations (0.1%).

Table 17: Cost per day per prescriptions in various respiratory diseases
(n=1000)

	Minimum	Maximum	Mean	SD
Total Population	6.9	80.9	44.9	21.0
Bronchial Asthma	8.6	80.1	45.6	22.1
COPD	8.4	80.7	46.1	20.8
COVID-19	8.3	80.9	46.2	19.9
ILD	10.1	77.2	46.3	21.6
Pneumonia	8.1	80.7	46.7	22.4
Post Covid Fibrosis	31.2	66.6	46.7	18.1
Tuberculosis*	8.1	80.2	44.7	21.6
URTI	6.9	78.9	41	20.5
Miscellaneous	23.4	77.7	46.7	21.4

*Does not include cost of ATT

The mean (SD) cost of drug per dosage per day of prescriptions irrespective of the disease was ₹44.9 (21), with a minimum of ₹ 6.9 and a maximum of ₹80.9.

Table 18: Cost per day of prescriptions in covid vs non covid cases (n=1000)

Variable	Condition		t-test	P value
	Covid	Non-Covid		
Cost per day per prescription	44.42 (21.23)	46.63 (19.8)	-1.340	0.180

The cost per day of prescription among the non-covid patients was slightly higher than the covid patients. However, this difference was not statistically significant.

DISCUSSION

Drug utilisation studies are used to measure the performance of healthcare providers in fostering the appropriate use of drugs. The drug use indicators can serve to focus attention on one or two aspects of performance, narrowing down the area of subsequent inquiry.[xxv] Assessing the prescribing practice of health institutions can be used as baseline data for further interventional studies.[xxxvii]

The present study collects prescription from the department of department of pulmonary chest and TB of a tertiary care hospital, to assess the patterns of drugs prescribed, their doses & duration, for covid and non-covid patients, and to assess the pattern of drugs prescribed and adverse drug reactions.

For the present study, a total of 1280 prescriptions were collected from the pulmonary medicine units of the Santosh Medical College and Hospital, during the Study duration. Several of these prescriptions had improper or incomplete entries. In the final analysis only patients with a completely correct prescription (1000) were included for analysis. As a proportion of all samples collected the errors in prescription as compared to other studies have been summarised in the table below.

Table 19: Comparison of certain parameters among studies (n=1000)

Parameters	Present study	Albarrak et al [xxxviii]	Mengistu et al [xxxix]
Improper or omitted dose	126 (9.8%)	24 (12.1%)	17.1%
Improper or omitted frequency	21 (1.6%)	6 (3.0%)	6.7%
Improper or omitted route of administration	111 (8.7%)	30 (15.1%)	-
Incorrect treatment duration	0	5 (2.5)	-19.9%
Medical duplication	12 (0.9%)	4 (2%)	-
Drug interactions	10 (0.8%)	2 (1%)	-
Total errors	280 (21.9%)	71 (3.7)	-

Mengitsu et al,[xxxix] reported that dose of drugs were written in only 82.9% of prescription papers; which is lower than findings from Dilla, Ethiopia (94.9%) and Jimma, Ethiopia (89.8%) but higher than many findings from similar studies conducted in Sudan and Ethiopia which reported a range between 27.4% and 81.2%.[xl,xli,xlii,xliii,xliv,xlv] the authors also reported that the route of drug administration was written in 82.2% of prescription papers which was relatively comparable with previous findings from Harar, Ethiopia (81.8%) but lower compared to other similar studies which reported between 87.6–93.1%.[xliii,xlvi,xlvii]About 93.3% prescription papers revealed frequency of drug administration, which is higher than previous similar studies conducted at different corners of Ethiopia with a percentage report of 6.4–92.2%.[xl,xli,xlii,xlvi] Percentage of prescription papers with duration of treatment mentioned was 80.1%, a finding comparable with the study conducted in Gondar, Ethiopia (82%).[xli] However, this finding is higher than findings from other studies (20–74.6%).[xl,xlii,xliii,xliv,xlvi,xlviii]

In the present study, of all complete prescriptions studied 79.7% were from non-covid patients, while 20.3% of the prescriptions were from covid patients.

Characteristics of non-covid respiratory patients

About half the patients (49.3%), whose prescriptions were included in the study, in both the non-covid and covid groups, and overall were more than 60 years old, while the least proportion of patients were in the 18-30 years age group. In their study of 423 prescriptions given to non-covid patients with respiratory tract infections, attending General Medicine and Pulmonary Medicine OPDs, Kumar et al,[xlix] reported 64% were males and 36% were females. This is similar to the studies conducted by S. Ganesh kumar *et al* and Jadhav *et al* who also reported increased number of males when compared to females in their study.[l,li] The most commonly affected patients belonged to > 60 yrs age group which is similar to studies conducted by Mirza *et al* and Mahajan *et al*.[x,lii]

In the present study , among patients attending the outpatient department, one-fifths were covid patients, while the other four-fifths were non-covid patients. Among non-covid patients, the commonest diagnosis was chronic obstructive pulmonary disease (COPD) in 28%, followed by upper respiratory tract infection (URTI) in 19%, bronchial asthma in 18%, tuberculosis in 11%, community acquired pneumonia in 3% and miscellaneous in 1%, which included 6 patients with interstitial lung disease (ILD), 3 patients with lung masses for evaluation and 1 patient with sarcoidosis. Dasgupta et al,[xxxi] reporting from a referral chest clinic found that most patients were asthma (26.5%) followed by COPD (12.2%), tuberculosis (7.3%) and other infective problems (7.2%) such as pneumonia and bronchiectasis. other problems like ILD (4.32%), pleural diseases (2.78%) and sarcoidosis were reported less frequently. Kumar et al, reported that the most

common respiratory tract infections for which the patient came to the hospital were chronic obstructive pulmonary disease (34.98%), pulmonary tuberculosis (33.33%), bronchial asthma (16.78%), lower respiratory tract infections (8.03%) and upper respiratory tract infections (6.85%). These findings are in accordance with the other previous studies done on respiratory tract infections.[x,lii,liii] In another study, Beg et al,[x] the most common diseases were chronic obstructive pulmonary disease (COPD), Pulmonary tuberculosis, Bronchial asthma, Pneumonia and upper respiratory tract infections (URTIs), which is similar to the previous studies.[lii,liii]

Characteristics of covid patients

Among the patients included in the covid group, in the present study, the mean (standard deviation) age was 49.2 (16.8) years, the minimum was 22 years, while the maximum was 78 years. Most (50.9%) were females. Among covid patients, the majority were (65.5%). In their retrospective study on drug utilisation among 1532 individuals who tested positive for COVID-19, in Italy, Orlando et al,[liv] noted that most of the patents in the cohort comprised middle-aged men (55 ± 19 years of whom 80% were > 40 years of age, and males, who comprised 60.9% of the cohort. Of the 203 covid patients included in the present study 3 (1.5%) were being treated for post covid fibrosis.

Common co-morbidities in covid and NCRP

In the present study, the most common recorded co-morbidity among all prescriptions was hypertension (25.3%), while the least common was Rheumatoid arthritis (0.3%). Among non-covid patients the commonest recorded co-morbidity was hypertension (22.1%) followed by diabetes (16.6%). Among covid patients also the commonest comorbidity was hypertension (37.9%) and diabetes (10.4%). In their study on 144 hospitalised covid 19 patients from AIIMS,

New Delhi, in 2020, Mohan A et al, reported comorbidities 23 in 15.9% of all patients, with diabetes mellitus in 11.1% and Hypertension in 2.1%., bronchial asthma and concomitant pulmonary tuberculosis in in 0.7% of the cases.[lv] Sun et al,[xxxvi] reported that the most common comorbidities were hypertension (24.8%), cardiovascular disease (9.7%), diabetes (7.3%), and cancer (4.8%). Almost half (42.3%) of patients theta died due to covid 19 in Indonesia between March and September 2020, had co-morbid hypertension (42.3%), cardiovascular disease (30.8%), diabetes (28.2%), or other comorbidities, alone or in combinations.[lvi]

A thorough search of the literature failed to reveal any paper on the co-morbidity profile of patients attending a respiratory medicine OPD, for reasons other than Covid 19. However, some studies provide some indirect insights into the profile of co-morbidities among patients with NCRD. A study by Butler et al, [lvii] studied the presence of comorbid conditions in patients on pulmonary rehabilitation (PR) programmes. They reported that circulatory (64%) and endocrine/metabolic (45%) conditions were most common in COPD. In ILD, digestive (55%) and circulatory (53%) comorbidities were most prevalent. Incalzi et al,[lviii] while assessing a group of COPD patients found that the most common co-morbid diseases were, hypertension (28%), diabetes mellitus (14%), and ischaemic heart disease (10%).

Prescriptions for covid patients

We also found that the prescriptions were diverse in practice, and most of the medications were prescribed considering the patient's characteristics, including disease severity, ageand the presence of comorbidities. The clinical features of patients with COVID-19 in our study were similar to other studies, with fever as the predominant symptom.[lix,lx] Among prescriptions for

covid patients, antibiotics and antipyretics were prescribed in 98.5% and 96.1% of cases, which is almost universal in use.

The most commonly prescribed antibiotic was doxycycline (98.5%), in-line with the recommendations at the time of the study. Amoxycillin+ clavulanic acid and azithromycin were used in 21.2 and 40.4% of these patients together with doxycycline. The use of antibiotics, especially some that the World Health Organization recommends reserving for the most difficult-to-treat cases, may be "adding fuel to the fire of the already alarming antimicrobial resistance levels," Kamini Walia, a microbiologist with the Indian Council of Medical Research, and colleagues said Monday in a study. "Fear of missing a secondary infection and lack of specific therapy for Covid-19 leads to over-prescription of antibiotics".[lxi]

Other commonly used medications were anti-histaminics (81.1%), ivermectin and vitamins and zinc (78.8%). Inhaled corticosteroids were used in 11.8%, while oral corticosteroids were used in 1.5% of the patients.

In the cohort of patients reported by Sun et al,[xxxvi] nearly all patients in this study received anti-bacterials, 92.7% received antivirals, and 69.7% received glucocorticoids. The lower prescription of antibiotics and glucocorticoids in patients in the present study could be due to a lower age group of patients, and hence lesser disease severity and co-morbidity.[lix,lxii,lxiii]

Prescriptions for non covid respiratory patients

In the present study, the most commonly prescribed drug group was mucolytics (94%) followed by antibiotics (85.8%), inhaled corticosteroids (77.8%) and inhaled bronchodilators (59.2%). Antitubercular drugs were prescribed in 14.1% of the patients. Despite a thorough search of the

existing literature, a similar study looking into the prescribing patterns among patients attending the outpatient department of pulmonary medicine could not be found. The nearest was the study by Kumar et al,[xlix] who looked into the prescription pattern of drugs given to patients with respiratory tract infections visiting General Medicine and Pulmonary Medicine Out Patient Department of a tertiary care hospital. Similar to the present study, they reported that mucolytics expectorants (18.87%) were the most commonly prescribed group of drugs followed by antibiotics (18.28%), bronchodilators (14.78%), corticosteroids (14.02%) and others in patients although the proportions were much lower than the present study. Jadav et al,[li] studied prescriptions from children between one and five years of either sex, suffering from acute respiratory tract infections, and found that the most common drugs used were from antipyretic group, with 98.3% of them receiving at least one antipyretic. This might be because the study was done in children of one to five years, whose most common presenting symptom for respiratory tract infection is fever. Since adult patients were included in the present study mucolytics and expectorants would have been given to bring symptomatic relief in these patients.

Beg *et al*,[x] described high proportion of antibiotics use among patients with respiratory tract infections. In the present study antibiotic prescription was higher than that reported by Mirza et al.[x] Given the fact that many of the exacerbations in respiratory illnesses especially asthma is viral in origin, this high and unnecessary use of antibiotics increases the chances of development of antibiotic resistance in future.

Like in the study by Kumar et al,[xlix] vitamin and mineral supplements Vitamin D and Calcium tablets were also given in our study. These must have been prescribed to improve appetite,

generalized fatigue and weakness associated with the illness. Among the mucolytics, various combinations of acetylcysteine and bromhexine were most commonly prescribed which does not match with any study conducted till date.

Table 20: WHO core prescribing indicators (non-covid patients)

WHO core prescribing indicators	WHO recommended values	Present study	Kumar et al[xlix]	Pramil et al[lxiv]	Gogoi et al[lxv]
Average number of medicines per encounter	1.6-1.8	5.2	5.59	2.4	6.92
Percentage of encounters with an antibiotic	20-26.8%	85.6%	94%		100%
Percentage of encounters with an injection	13.4-24.1%	0%	2.32%		-
Percentage of medicines prescribed by generic name	100%	21.7%	19.3%		0%
Percentage of medicines prescribed from essential medicine list (EML)	100%	100%	40.09%		-

The number of drugs prescribed per prescription is a major component of the prescribing indicators and can provide basic knowledge about the prevalence of poly-pharmacy among the healthcare professionals in a region. As per the WHO standards, a value of 1.6-1.8 drugs per encounter is optimal.[lxvi] However, this value varies widely not only in different countries around the globe but in different regions of the same country. For example, in countries like Ethiopia,

Sudan and Zimbabwe the average number of drugs per prescription varies from 1.3-1.6, while in countries like Iran or Nigeria it is more than double, and even reaches as high as 3.8.[lxvii,lxviii,lxix,lxx,lxxi] Regional variations within the country has been demonstrated in prescriptions from various parts of India, with value varying between 2.7 and 3.2.[lxxii,lxxiii,lxxiv,lxxv]

Kumar et al,[xlix] described an average of 5.59 drugs was prescribed per prescription in patients with respiratory tract infection attending a tertiary care outpatient clinic. In a study by Gogoi et al,[lxv] an overall antibiotic prescription rate for patients with URTI was 100% i.e. every prescription had one antibiotic prescribed in it which is very high for treating diseases with an overwhelmingly viral aetiology (>85% in some studies). Antibiotic prescription rates of 86.6% has been reported from Thailand,[lxxvi] 60% in Japan,[lxxvii] 57% in Denmark,[lxxviii] 65% in Spain,[lxxviii] and 38%, in the USA has been reported.[lxxix] A low rate (18%) of antibiotic prescription for URTI was shown in one study conducted by Gjelstad S et al in Norway.[lxxx] These studies show that antibiotic prescription rate for URTI is high in both developing and developed countries in Asia as well as in South Europe, compared with low rates in Scandinavian countries and most hospitals in the United States.[lxv]

In the present study the higher average of drugs used could be due to the increased number of patients with severe disease referred to the tertiary care centre. In addition, increasing age of the attendees were associated with increased co-morbidities that demanded more medicines to treat.

Proportion of drugs prescribed in generic terms

Percentage of drugs prescribed by generic name in the present study was 32.1%, (42.2% of covid and 29.4%0 of NCRP which is less than the WHO standard, requiring all drug prescriptions to be written in generic names. No available study on the internet has specifically looked into generic

prescription of drugs among covid or NCRP patients. However, one study by Jadhav S el al,[li] among in children aged 1 to 5 years, with respiratory infections, at a tertiary care teaching hospital, in Maharashtra, reported no single drug was prescribed by generic name. Studies form West Bengal, on general outdoor prescriptions have shown a significant increase in the rate of prescription of generic drugs from 38% in 2007[lxxii] to 95.3% in 2017.[xxxv] This can be attributed to the guidelines issued by the Medical Council of India in 2013 and the growing awareness among the healthcare practitioners.[lxxxi]

Table 21 : WHO core prescribing indicators (covid patients)

WHO core prescribing indicators	**WHO recommended values**	**Present study**	**Sun et al[xxxvi]**
Average number of medicines per encounter	1.6-1.8	5.5	
Percentage of encounters with an antibiotic	20-26.8%	98.5%	98.8%
Percentage of encounters with an injection	13.4-24.1%	0.0%	-
Percentage of medicines prescribed by generic name	100%	32.1%	-
Percentage of medicines prescribed from essential medicine list (EML)	100%	100%	-

Proportion of prescriptions with injections

In the present prescription study, none of the patients were prescribed injectables, which is well below the maximum recommended value, probably because of the study setting, which is a specialised outpatient department, where diseases requiring parenteral drugs are not commonly encountered. Per prescriptions is expected to be much higher.

Adverse reactions to drugs

In the present study, slightly more than a quarter (22.1%) of the study population had some adverse effects to the drugs prescribed. The commonest side effect recorded on the prescription was diarrhoea (7%), followed by nausea/ vomiting (6.5%), urticaria (6%), cough (2.8%) and dizziness (2.6%). The least common recorded adverse drug reaction on prescriptions was palpitations (0.1%).

Prescription costs

In the present study, the mean cost of prescriptions among NCRP patients was ₹46.63 (19.8) while that among covid patients was ₹44.42 (21.23) With current advances in the field of medicine, a growing concern among the global populace is the ballooning of healthcare costs. One of the most important determinants of this problem is the practice of prescribing drugs and formulations by their brand-names rather than their generic names by the physicians, the prices of the former being substantially higher.[lxxxii] This often make essential drugs out of reach for patients in the lower socio-economic strata, who are the ones that are the most vulnerable to all forms of diseases and are in most need of these drugs. This problem is especially alarming in the developing and transitional countries of the world, such as India.[lxxxiii] The study found that 18.1% of the total drugs prescribed were prescribed in their generic names, and much lower than that found in West Bengal (38%) and studies done in other countries like Nepal (13%) and Nigeria (54%).[lxxii,lxxxiv.,lxxxv]

Limitations

- Although the sample size was adequate, the results of the study have limited generalizability as all information were obtained from a single institution. There is a need for multicentre research with larger sample size and longer follow-up period in the future in order to promote a more solid basis for medication recommendations.
- The present study did not include patients that were admitted with covid pneumonia.

SUMMARY

Introduction

Pulmonary disease, including covid 019, in India is widespread. Despite that, there has been a dearth of study regarding the drug utilization and rationale of the same., in India.

Objectives

The objectives of the present study were as follows

- To assess the most frequently prescribed drugs and their doses & duration for conditions including COPD, Tuberculosis, Bronchial Asthma, pneumonia, Covid-19 and post COVID fibrosis.
- To assess the pattern of drugs prescribed in the department of pulmonary chest and TB.
- To assess cost analysis per prescription.
- To assess ADR if any observed.

Materials and Methods

The present study was an observational, cross-sectional type of study conducted in the department of Pharmacology and Pulmonary medicine of a tertiary care hospital, on 1000 prescriptions from covid and non-covid patients after checking the inclusion and exclusion criteria. All consecutive prescriptions generated at the department of Pulmonary medicine were included on fulfilling the eligibility criteria. The study was approved by the Institution Ethics Committee (IEC).

Collected data from all participants were checked for consistency and completeness, entered in into Microsoft Excel and analysed using IBM statistical package for Social Sciences (SPSS) version 21.0.

Results

- The totals of 1280 prescriptions were taken up for the study, of which 280 were discarded due improper doses (126), improper or omitted frequency (21), improper or omitted route of administration (111), medical duplication (12) and drug interactions (10).
- Majority (79.7%) of the prescriptions are from NCRP, while 20.3% of the prescriptions are from covid patients.
- One-fifths (20%) of the prescriptions included in the study were from covid patients, while the others were from non-covid patients. Among them the commonest prescriptions (28%) were from COPD patients, followed by URTI (19%). The lowest number of patients had miscellaneous diagnosis like interstitial Lung disease, lung cancers etc.

- Among the total prescriptions, most were more (49.3%) than 60 years of age. Among both covid and non- covid respiratory patients, the highest proportion of patients were more than 60 years old (54.1 and 30.5% respectively).
- The mean (standard deviation) age of patients in total, non-covid respiratory and covid prescriptions were 55.9 (17.7), 57.5 (17.5) and 49.2 (16.8) years respectively.
- Among the total prescriptions, most (50.9%) were females. Among non-covid respiratory patients majority were female (55.1%) while among covid patients majority were males (65.5%)
- The most common recorded co-morbidity among all prescriptions was hypertension (25.3%), while the least common was Rheumatoid arthritis (0.3%). Among non-covid patients the commonest recorded co-morbidity was hypertension (22.1%) followed by diabetes (17.7%). Among covid patients also the commonest comorbidity was hypertension (37.9%) and diabetes (10.4%).
- Antibiotics were prescribed in 88.2% of total, 85.6% of non-covid cases and 98.5% of all covid cases respectively.
- Overall, the most commonly prescribed drug group was mucolytics (94%) followed by antibiotics (88.2%), inhaled corticosteroids (64.4%) and inhaled bronchodilators (50.2%).
- No antibiotics were prescribed in 11.6%, 14.2% and 1.5% of patients in overall prescriptions, non -covid prescriptions and covid prescriptions respectively.
- Most commonly prescribed antibiotics in the prescriptions of covid patients is doxycycline (98.5%) followed by Azithromycin (40.4%) and in NCRP is Amoxicillin+clavulanic acid (27.6%) followed by ciprofloxacin, azithromycin, and doxycycline.
- Among non-covid prescriptions, the most commonly prescribed drug group was mucolytics (94%) followed by antibiotics (85.6%), inhaled corticosteroids (77.8%) and

inhaled bronchodilators (59.2%). Antitubercular drugs were prescribed in 14.1% of the patients.

- Among prescriptions for covid patients, the most commonly prescribed drug groups were antibiotics and antipyretics (98.5%) followed by antihistaminic (81.1%), ivermectin and vitamins and zinc (78.8%).
- Overall, the most prescriptions had 5-6 drugs (50.9%). For both non-covid and covid patients, the most prescriptions had 5-6 drugs, 53.7% and 55.6%, respectively.
- The mean (standard deviation) number of drugs per prescription overall, among non-covid prescriptions and covid prescriptions were 5.2, 5.1 and 5.5 respectively.
- The mean (standard deviation) number of generic drugs per prescription overall, among non-covid prescriptions and covid prescriptions were 2.3(1.0) and 1.5 (1.0) respectively.
- Adverse reactions were observed in 22.1% of the total patients. The commonest adverse reaction recorded on the prescription was diarrhoea (7%), followed by nausea/ vomiting (6.5%), urticaria (6%) and dizziness (2.6%). The least common recorded adverse drug reactions on prescriptions were drowsiness, elevated liver enzymes (0.2%) and palpitations (0.1%).
- The mean (SD) cost of drug per dosage per day of prescriptions irrespective of the disease was ₹44.9 (21), with a minimum of ₹ 6.9 and a maximum of ₹80.9.
- The cost per day of prescription among the non-covid patients was slightly higher than the covid patients. However, this difference was not statistically significant.

CONCLUSION

In this study Drug utilization study of drugs prescribed in covid and non-covid respiratory patients were evaluated in prescriptions of patients who attended OPD in the department of pulmonary medicine at a tertiary care teaching hospital.

The era of the covid-19 pandemic was an unpredictable era for the modern medicine in the whole world. The covid-19 pandemic has placed a huge burden on health systems worldwide. The existing systems were undoubtedly not ready to handle an emergency of such large proportions and with such unpredictable characteristics. Unavailability of the direct anti-viral drugs led to repurposing of the drugs. Irrational prescribing of antibiotics was seen in prescriptions of covid-19 as well as in NCRP. This irrational use of antibiotics can lead to the resistance to antibiotics in the community.

The percentage of antibiotics prescribed in this study was unacceptably high i.e., 88.4% (85.8% in NCRP and 98.5% in covid) compared to the WHO standard (20 – 26.8%). The overuse of antibiotics and the consequential development of resistance to antibiotics is a global problem. Therefore, it is important to look seriously into the rational use of antibiotics and it is recommended to adhere to the guideline for the prescribing antibiotics. The value of PDD/DDD ratio >1 for most of the antibiotics in the study group also indicates that there is overdosing of the antibiotics, and physicians could be sensitized to assess and improve the prescribing pattern of the drugs.

This drug utilization pattern study also revealed deviation of the average number of drugs (5.2% in NCRP AND 5.5% in covid) per prescription from the WHO standard recommendation which is 1.6 to 1.8 drugs per prescription. In 47.9% of prescriptions, the presence of comorbidities is positively associated with polypharmacy. In the 52.1% of prescriptions which is not associated with any comorbidities, polypharmacy has a number of disadvantages like high healthcare costs, poor patient compliance, higher frequency of adverse effects, and drug-drug interactions. Hence, it is necessary to identify predictors of polypharmacy and bring amendments in prescribing practices.

The total percentage of prescriptions prescribed by generic name was 32.1% which is extremely less than what WHO recommends which is 100%. Prescribing by brand names can pose an unnecessary cost, difficulty remembering the name of the drug, accessibility issues, and bioequivalence mismatches. The solution to these problems is to promote prescription writing by generic names that avoid the risks associated with prescribing by brand name.

100% of drugs were prescribed from National Essential Drugs List and fulfilled the criteria of WHO recommendation that is 100%.

This study clearly showed that respiratory disease drug therapy needs to be continuously evaluated to encourage the more rational prescribing, for educating the patient's drug usage, to decrease morbidity and cost of therapy for the patient. Hence, there is a need to bring changes in the prescribing practices with particular emphasis on generic drug prescribing and restricting polypharmacy. Also, some amendments need to be incorporated in the hospital antibiotic policy to decrease antibiotic resistance. Such drug utilization studies are necessary to improve prescribing, administration, to minimize adverse events and promote rational use of medicines.

REFERENCES

[i] De Vries TP, Henning RH, Hogerzeil HV, Fresle DA, Policy M, World Health Organization. Guide to good prescribing: a practical manual. World Health Organization; 1994.

[ii] Wade O. Drug utilization studies: implications for medical care. Acta Medica Scandinavica. 1984:7-9.

[iii] Lars J. Auditing Drug Therapy: Approaches Towards Rationality At Reasonable Costs: Approaches Towards Rationality At Reasonable Costs. Taylor & Francis; 1992 Jan 31.

[iv] Consumption of drugs. Report on a symposium in Oslo 1969. Copenhagen, WHO Regional Office for Europe, 1970 (EURO 3102)

[v] Ghoshal AG, Ravindran GD, Gangwal P, Rajadhyaksha G, Cho SH, Muttalif AR, Lin HC, Thanaviratananich S, Bagga S, Faruqi R, Sajjan S. The burden of segregated respiratory diseases in India and the quality of care in these patients: Results from the Asia-Pacific Burden of Respiratory Diseases study. Lung India: official organ of Indian Chest Society. 2016 Nov;33(6):611.

[vi] Salvi S, Kumar GA, Dhaliwal RS, Paulson K, Agrawal A, Koul PA, Mahesh PA, Nair S, Singh V, Aggarwal AN, Christopher DJ. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990–2016. The Lancet Global Health. 2018 Dec 1;6(12):e1363-74.

[vii] Behera D, Sharma PP. A retrospective study of seasonal variation in the number of cases diagnosed at a tertiary care tuberculosis hospital. Indian J Chest Dis Allied Sci. 2011;53:145–52.

[viii] Chowdhury R, Mukherjee A, Naska S, Adhikary M, Lahiri SK. Seasonality of tuberculosis in rural West Bengal: A time series analysis. International Journal of Health & Allied Sciences. 2013 Apr 1;2(2):95.

[ix] Vinutna G, Babji M, Namburi R, Kumari R. Drug utilization study in patients with acute respiratory tract infections at a tertiary care hospital in Bhimavaram, India. International Journal for Advance Research and Development. 2018;3(9):35-44.

[x] Beg MA, Dutta SB, Bawa S, Kaur A, Vishal S, Kumar U. Prescribing trends in respiratory tract infections in a tertiary care teaching hospital. International Journal of Research in Medical Sciences. 2017 Jun;5(6):2588-91.

[xi] Wadud A, Prasad PV, Rao MM, Narayana A. Evolution of drug: a historical perspective. Bull Indian Inst Hist Med Hyderabad. 2007 Jan 1;37(1):69-80.

[xii] Newton P. The use of medicinal plants by primates: A missing link?. Trends in Ecology & Evolution. 1991 Sep 1;6(9):297-9.

[xiii] Engel A, Siderius P. The consumption of drugs. Report on a study 1966-1967. Copenhagen, WHO Regional Office for Europe, 1968 (EURO 3101).

[xiv] Bergman U, Elmes P, Halse M, Halvorsen T, Hood H, Lunde PK, Sjöqvist F, Wade OL, Westerholm B. The measurement of drug consumption. European journal of clinical pharmacology. 1975 Mar;8(2):83-9.

[xv] Bergman U, Gr'imsson A, Wahba AH, Westerholm B, World Health Organization. Studies in drug utilization: methods and applications. World Health Organization. Regional Office for Europe; 1979.

[xvi] Stika L et al. Organization of data collection in Czechoslovakia. In: Bergman U et al., eds. Studies in drug utilization. Methods and applications. WHO Regional Office for Europe, Copenhagen, 1979 (WHO Regional Publications European Series No. 8) pp.125-136.

[xvii] Baksaas Aasen I. Drug dose statistics, listof defined daily doses for drugs registered in Norway. Oslo, Norsk Medicinal Depot. 2015.

[xviii] WHO. Introduction to drug utilization research. Geneva: World Health Organization; 2003.

[xix] Laporte JR, Porta M, Capella DO. Drug utilization studies: a tool for determining the effectiveness of drug use. British journal of clinical pharmacology. 1983 Sep;16(3):301-4.

[xx] Bergman U, Popa C, Tomson Y, Wettermark B, Einarson TR, Åberg H, Sjöqvist F. Drug utilization 90%–a simple method for assessing the quality of drug prescribing. European journal of clinical pharmacology. 1998 Apr;54(2):113-8.

[xxi] Einarson TR, Bergman U, Wiholm BE. Principles and practice of pharmacoepidemiology. Avery's drug treatment: a guide to the properties, choice, therapeutic use and economic value of drugs in disease management. 1997;4:371-92.

[xxii] Lee D, Bergman U. Studies of drug utilization. In: Strom B ed. Pharmacoepidemiology, 3rd ed. Chichester, J Wiley, 2000:463-481.

[xxiii] Baksaas I. Patterns in drug utilization – national and international aspects: antihypertensive drugs. Acta Medica Scandinavica, 1984, suppl. 683:59-66.

[xxiv] Bergman U et al. Auditing hospital drug utilization by means of defined daily doses per bedday. A methodological study. European Journal of Clinical Pharmacology, 1980, 17:183-187.

[xxv] World Health Organization. How to investigate drug use in health facilities: Selected drug use indicators. Geneva,World Health Organization, 1993 (unpublished document WHO/DAP/93.1;

available on request from Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva, 27, Switzerland)

[xxvi] Laing RO. Rational drug use: an unsolved problem. Tropical doctor. 1990 Jul;20(3):101-3.

[xxvii] Walker GJ, Hogerzeil HV, Sallami AO, Ala'din AS, Fernando G, Kassem FA. Evaluation of rational drug prescribing in Democratic Yemen. Social Science & Medicine. 1990 Jan 1;31(7):823-8.

[xxviii] Christensen RF. A strategy for the improvement of prescribing and drug use in rural health facilities in Uganda. Ugandan Essential drugs and management program. 1990 Sep;2.

[xxix] World Health Organization. The rational use of drugs. 1986.

[xxx] India State-Level Disease Burden Initiative CRD Collaborators. The burden of chronic respiratory diseases and their heterogeneity across the states of India: The global burden of disease study 1990-2016. Lancet Glob Health. 2018 pii: S2214-109X(18)30409-1.

[xxxi] Dasgupta A, Bagchi A, Nag S, Bardhan S, Bhattacharyya P. Profile of respiratory problems in patients presenting to a referral pulmonary clinic. Lung India: Official Organ of Indian Chest Society. 2008 Jan;25(1):4.

[xxxii] Jindal SK. Emergence of chronic obstructive airway disease as on epidemic in India. Ind J Med Res 2006; 124: 619-630

[xxxiii] Chowgule R, Shytye VM, Parmer RJ, Bhosale AM, Khandagale MR, Phalnitkar SV,et al. Prevalence of respiratory symptoms, bronchial hyperreactivity and asthama in a mega city: results of the European community Respiratory health survey in Mumbai. Am J Respir Crit Care Med 1998; 158: 547-554

[xxxiv] Dubey A, Sharma P. Profile of respiratory problems in patients attending a tertiary care center OPD - A study from central India. Int J Med Res Rev [Internet]. 2015Aug.31 [cited 2022Oct.17];3(7):743-7. Available from: https://ijmrr.medresearch.in/index.php/ijmrr/article/view/313

[xxxv] Bandyopadhyay A, Dhar D, Mukherjee A, Bhattacherjee S, Dasgupta S. Practices regarding prescription and dispensing of drugs in a tertiary care hospital in rural West Bengal, India. Int J Basic Clin Pharmacol. 2017 Nov;6(11):2712-7.

[xxxvi] Sun F, Kou H, Wang S, Lu Y, Zhao H, Li W, Zhou Q, Jiang Q, Cheng Y, Yang K, Zhuo L. An analytical study of drug utilization, disease progression, and adverse events among 165 COVID-19 patients. Annals of Translational Medicine. 2021 Feb;9(4).

[xxxvii] West SL, Strom BL, Freundlich B, Normand E, Koch G, Savitz DA. Completeness of prescription recording in outpatient medical records from a health maintenance organization. *J Clin Epidemiol*. 1994;47 (2):165–171. doi:10.1016/0895-4356(94)90021-3

[xxxviii] Albarrak AI, Al Rashidi EA, Fatani RK, Al Ageel SI, Mohammed R. Assessment of legibility and completeness of handwritten and electronic prescriptions. Saudi Pharmaceutical Journal. 2014 Dec 1;22(6):522-7.

[xxxix] Mengistu G, Misganaw D, Tsehay T, Alemu BK, Bogale K. Assessment of Drug Use Pattern Using WHO Core Prescribing Indicators at Outpatient Settings of Governmental Hospitals in Dessie Town. Drug, Healthcare and Patient Safety. 2020;12:237.

[xl] Gashaw T, Sisay M, Mengistu G, Amare F. Investigation of prescribing behavior at outpatient settings of governmental hospitals in eastern Ethiopia: an overall evaluation beyond World

Health Organization core prescribing indicators. *J Pharm Pol Pract*. 2018;11(1):26. doi:10.1186/s40545-018-0152-z

[xli] Admassie E, Begashaw B, Hailu W. Assessment of drug use practices and completeness of prescriptions in Gondar University Teaching Referral Hospital. *Int J Pharm Sci Res*. 2013;4(1):265.15

[xlii] Asrade B. Assessment of completeness of prescription and rational drug use practice at Felege Hiwot Referral Hospital, North West Ethiopia. *Assessment*. 2019;60.

[xliii] Ayele T, Tsehay T, Bedada H. Prescribers' adherence to the basic principles of prescription order writing in a teaching hospital, Ethiopia. *Indo Am J Pharm Res*. 2017;7(8):499–503.

[xliv] Yilma Z, Mekonnen T, Siraj EA, et al. Assessment of prescription completeness and drug use pattern in Tibebe-Ghion comprehensive specialized Hospital, Bahir Dar, Ethiopia. *Biomed Res Int*. 2020;2020.

[xlv] Rabie D, Kheder SI. Assessment of prescribing and dispensing practices based on WHO core prescribing indicators in hospital and community pharmacies in Khartoum State-Sudan. *J Med Inf Decision Making*. 2020;1(3):1. doi:10.14302/issn.2641-5526.jmid- 20-3493

[xlvi] Bekele NA, Tadesse J. Prescription auditing based on world health organization (WHO) prescribing indicators: a case of Dilla university referral hospital. *J Drug Del Ther*. 2018;8(6–s):21–25. doi:10.22270/ jddt.v8i6-s.2165

[xlvii] Melaku T, Molla G. Assessment of prescribers' adherence to the basic standards of prescription order writing in jimma university specialized Hospital, Southwest Ethiopia. *Southwest Ethiopia: The Experiment*. 2014;19(1):1316–1329.

[xlviii] Shelat PR, Kumbar SK. Analysis of outdoor patients' prescriptions according to World Health Organization (WHO) prescribing indicators among private hospitals in Western India. *J Clin Diagn Res*. 2015;9(3):FC01.

[xlix] Kumar RN, Selva P. Analysis of prescription pattern of antibiotics among patients with respiratory tract infections at a tertiary care hospital. Biomedical and Pharmacology Journal. 2019 Sep 25;12(3):1595-602.

[l] Kumar SG, Majumdar A, Kumar V, Naik BN, Selvaraj K, Balajee K. Prevalence of acute respiratory infection among under-five children in urban and rural areas of Puducherry, India. Journal of natral science, biology, and medicine.
2015; 6(1): 3.

[li] Jadhav S, Khanwelkar C. Prescribing Pattern of Drugs in Acute Respiratory Tract Infection in Children Aged 1 To 5 Years At Tertiary Care Teaching Hospital. Biomedical and Pharmacology Journal. 2018 Dec 25;11(4):1903- 11.

[lii] Mahajan HM, Date AP, Badwaik RT, Borkar AS, Wanmali SS, Gohad GV. Analysis of Pattern of Antimicrobial use in Respiratory Tract Infections in a Tertiary Care Hospital of Central India-A Drug Utilization Study. J Cont Med A Dent 2014; 2 (3):59-64.

[liii] Errabelly P, Ramavath V, Afreen A, Sanaboina A. Analysis of the prescribing pattern of antibiotics in respiratory tract infections at department of medicine at a tertiary care teaching hospital. IJPSR. 2015;6(7):2693-97.

[liv] Orlando V, Coscioni E, Guarino I, Mucherino S, Perrella A, Trama U, Limongelli G, Menditto E. Drug-utilisation profiles and COVID-19. Scientific reports. 2021 Apr 26;11(1):1-0.

[lv] Mohan A, Tiwari P, Bhatnagar S, Patel A, Maurya A, Dar L, Pahuja S, Garg R, Gupta N, Sahoo B, Gupta R. Clinico-demographic profile & hospital outcomes of COVID-19 patients admitted at a tertiary care centre in north India. The Indian journal of medical research. 2020 Jul;152(1-2):61.

[lvi] Djaharuddin I, Munawwarah S, Nurulita A, Ilyas M, Tabri NA, Lihawa N. Comorbidities and mortality in COVID-19 patients. Gaceta sanitaria. 2021 Jan 1;35:S530-2.

[lvii] Butler SJ, Li LS, Ellerton L, Gershon AS, Goldstein RS, Brooks D. Prevalence of comorbidities and impact on pulmonary rehabilitation outcomes. ERJ open research. 2019 Oct 1;5(4).

[lviii] Incalzi RA, Fuso L, De Rosa M, Forastiere F, Rapiti E, Nardecchia B, Pistelli R. Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease. European Respiratory Journal. 1997 Dec 1;10(12):2794-800.

[lix] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382:1708-20.

[lx] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497-506.

[lxi] Gale J, Shrivastava B. Excessive antibiotics use in Covid-19 cases adds 'fuel to fire' in India. Available at https://www.business-standard.com/article/current-affairs/excessive-antibiotics-usage-in-covid-cases-worsens-india-s-superbug-crisis-121052600099_1.html. Last accessed September 2022.

[lxii] Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ 2020;368:m606.

[lxiii] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.

[lxiv] Pramil T, Rajiv A, Gaurav G. Prescription practice in patients of upper respiratory tract infection at a pediatric outpatient clinic in Punjab. Indian Journal of Pharmacy Practice. 2014;7(2).

[lxv] Gogoi S, Saikia PP. A study on prescribing pattern of antibiotics for upper respiratory tract infections by general practitioners in rural areas of Assam. IJSR. 2015;4(5):60-2.

[lxvi] Isah AO, Ross-Degnan D, Quick J, Laing R, Mabadeje AF. The Development of Standard Values for the WHO Drug Use Prescribing Indicators. Nigeria: ICUM/EDM; 2004.

[lxvii] Abdulahi M, Shifera WT. Pattern of prescription in Jimma Hospital. Ethiop J Health Dev. 1997;11:263-7.

[lxviii] Bannenberg WJ, Forshaw CJ, Fresle D, Salami AO, Wahab HA. Evaluation of Nile Province Essential Drug Project. Geneva: WHO, WHO/91.10; 1991. Available at https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-017-2097-3.

[lxix] Ministry of Health/Zimbabwe Essential Drug Action Programme. Essential drug survey. Geneva: WHO, 74(WHO/93.1). 1993.

[lxx] Karimi A, Haerizadeh M, Soleymani F, Haerizadeh M, Taheri F. Evaluation of medicine prescription pattern using World Health Organization prescribing indicators in Iran: A cross-sectional study. J Res Pharm Pract. 2014;3:39-45.

[lxxi] Hogazeil HV, Bimo, D- Ross Degnan, Laing RO, Adjei DO, Santaso B, et al. Field test for rational drug use in twelve developing countries. Lancet. 1993;342:1408-10.

[lxxii] Sarkar AP, Biswas S, Tripathi SK. A study on drug use in a district hospital of West Bengal. Indian J Public Health. 2007;51(1):75-6.

[lxxiii] Gangopadhyay T, Mandal A, Mandal S, Basu B, Maiti T, Das A, et al. Drug utilization study from a government sponsored pharmacy in a tertiary care teaching hospital of rural West Bengal: a cross-sectional study. Int J Health Allied Sci. 2016;5:138-42.

[lxxiv] Vijaykumar TM, Sathyavati D, Subhashini T, Grandhi S, Dhanaraju MD. Assessment of prescribing trends and rationality of drugs prescriing. Int J Pharmacol. 2011;7:140-3.

[lxxv] Kumari R, Idris MZ, Bhushan V, Khanna A, Agarwal M, et al. Assessment of prescription pattern at the public health facilities of Lucknow district. Indian J Pharmacol. 2008;40:243-7.

[lxxvi] Thamlikitkul V, Apisitwittaya W. Implementation of clinical practice guidelines for upper respiratory infection in Thailand. Intern J Infect Dis. 2004; 8: 47-51.

[lxxvii] Higashi T, Fukuhara S. Antibiotic prescriptions for upper respiratory tract infection in Japan. Inter Med. 2009; 48:1369-75.

[lxxviii] Bjerrum L, Boada A, Cots JM et al. Respiratory tract infections in general practice: considerable differences in prescribing habits between general practitioners in Denmark and Spain. Eur J Clin Pharmacol. 2004; 60: 23-8.

[lxxix] Gonzales R, Camargo CA Jr, MacKenzie T et al. Antibiotic treatment of acute respiratory infections in acute care settings. Acad Emerg Med. 2006; 13:288-94.

[lxxx] Gjelstad S, Dalen I, Lindbaek M. GPs' antibiotic prescription patterns for respiratory tract infections still room for improvement. Scand J Prim Health Care. 2009; 27:208-15.

[lxxxi] Medical Council of India, Circular to the dean/principals of medical colleges regarding the prescribing drugs under their generic names, MCI-211(2) (Gen.)/2012-Ethics, (2013) Available at http://www.mciindia.org/tools/announcement/CircularEthics 21.01.2013.pdf. Retrieved on September 15, 2017.

[lxxxii] Haas JS, Phillips KA, Gerstenberger EP, Seger AC. Potential savings from substituting generic drugs for brand-name drugs: medical expenditure panel survey, 1997-2000. Ann Intern Med. 2005;142:891-7.

[lxxxiii] Kumar K, Singh A, Kumar S, Ram F, Singh A, Ram U, et al. Socio-Economic differentials in impoverishment effects of out-of-pocket health expenditure in China and India: evidence from WHO SAGE. PLoS ONE. 2015;10(8):e0135051. doi:10.1371/journal.pone.0135051.

[lxxxiv] Erah PO, Olumide GO, Okhamafe AO. Prescribing practices in two health care facilities in Warri, Southern Nigeria: A comparative study. Tropical Journal of Pharmaceutical Research. 2003;2(1):175-82.

[lxxxv][lxxxv] Ghimire S, Nepal S, Bhandari S, Nepal P, Palaian S. A prospective surveillance of drug prescribing and dispensing in a teaching hospital in Western Nepal. J Pak Med Assoc. 2009;59:726-31.